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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 08/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/799,941	WELCH ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005 and 14 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *9-16 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 1-8 and 17-22 and the protease inhibitor INVIRASE® in the replies filed on August 15, 2005 and February 14, 2006 are acknowledged.

Applicant has not indicated 'with' or 'without' traverse, nor has applicant did not distinctly and specifically point out the supposed errors in the restriction requirement. Therefore the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 9-16 and 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the replies filed on August 15, 2005 and February 14, 2006.

Claims 1-8 and 17-22 have been examined on the merits.

Information Disclosure Statement

The information disclosure statement filed July 12, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Specifically, references 4, 9, 14, 15, 27, 32, 35, 36, 47, 55, 57, 60, 65, 73, 76, 78, 80, 81, 87, 95, 97, 100, 101 and 103 have not been provided by Applicant for consideration.

Additionally, references 63 and 72 have not been considered as the citations on the IDS are incomplete.

Drawings

Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

Claims 2, 4 and 6 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims recite intended uses of the composition, however an intended use limitation does not distinguish the composition of the previous claim.

Applicant is advised that should claim 1 be found allowable, claims 2-7 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof.

Applicant is advised that should claim 8 be found allowable, claims 22 and 23 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof.

Applicant is advised that should claim 17 be found allowable, claims 18-20 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). As above, the intended use does not limit the composition and/or kit being claimed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112: .
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 17-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-8 and rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions/kits comprising oxytocin(OT) and secretin (S) for use in treating IBD, does not reasonably provide enablement for treating any other disorder or condition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (Wands, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to compositions and kits comprising oxytocin and secretin, optionally with a protease inhibitor. Thus, the claims taken together with the specification imply one could treat any GI, neurological or autoimmune disorder, as well as treating any 'pain' with OT/S, optionally with a protease inhibitor.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The MAYO CLINIC (Mayo Clinic. "CREST syndrome" internet document <http://www.mayoclinic.com/health/crest-syndrome/DS00580/DSECTION=8>, 6/3/05, 2 pages; accessed 8/24/06) teaches that in treating the calcinosis aspect of CREST syndrome, "Doctors have tried a number of drugs to treat calcium deposits with little success, although the antibiotic minocycline can sometimes reduce inflammation and ulcers in severe calcinosis." (page 1 of 2).

Furthermore, the MERCK Manual (Progressive Systemic Sclerosis (PSS) in The Merck Manual 16th edition (1992) R. Berkow, ed., pages 1321-1323) teaches that, in scleroderma (a

portion of CREST), "No drug has significantly influenced the natural history of PSS." (pages 1322).

The NIH News Alert (NIH News Alert. "The Use of Secretin to Treat Autism" internet document <http://www.nichd.nih.gov/new/releases/secretin.cfm> 8/17/01, 2 pages; accessed 8/24/06) teaches that, "Because its safety and efficacy have not been adequately tested for this purpose, the [NIH] does not currently have a formal position on the therapeutic use of secretin in the treatment of autism." (page 1 of 2). "Whether secretin will prove to be an effective treatment for autism and/or for GI disorders associated with autism cannot be determined at this time." (page 2 of 2).

ABOUT.com ("What drugs are used to treat autism?" internet document <http://autism.about.com/od/treatmentoptions/f/drugsfaq.htm> accessed 8/24/06, 1 page) teaches that, "there is no drug that directly treats autism as a syndrome," and that various drugs are generally prescribed to treat the symptoms, e.g. Zoloft or Prosac for anxiety, clonodine for behavioral issues.

ELLIS (C.R. Ellis, et al. "Autism" internet document <http://www.emedicinehealth.com/script/main/art.asp?articlekey=59039&pf=3&page=2> last edited 10/21/05, 11 pages; accessed 8/24/06) teaches that, "Although autism is the result of a neurologic abnormality, the cause of these problems with the nervous system is unknown in most cases." (page 2 of 11). "There is no lab test or X-ray that can confirm the diagnosis of autism." (page 5 of 11). "There is no cure for autism, nor is there a standard therapy that works for all people with autism." (page 6 of 11). "Medication does not treat the underlying neurological problems associated with autism. Rather, medication is given to help manage behavioral

manifestations of the disorder... Medication used in autism are psychoactive... [and] very few of these drugs have been tested in scientific studies in individuals with autism." (page 7 of 11).

HOLLANDER (US 2006/0105939 A1) teaches oxytocin for the treatment of autism (e.g. claim 1), though Hollander recognizes that, "Unfortunately, there are currently few treatment options for children and adults suffering from autism or disorders with similar behavioral characteristics." (paragraph [0010]).

Further, IBS (IBS and IBD: Two very different disorders. Internet document <http://www.ccfa/org/printview?pageUrl=/about/news/ibsoribd> posted 10/6/05, 3 pages; accessed 8/24/06) teaches that IBS and IBD, "are not the same condition, and they involve very different treatments." (page 1 of 3). "Symptoms can vary widely among individuals, but most IBS sufferers experience some degree of chronic and persistent abdominal pain, constipation, diarrhea, or constipation alternating with diarrhea.... Anemia, bleeding, weight loss, or fever—which may occur in IBD—are not symptoms of IBS." (page 1 of 3). Additionally, "The cause of IBS is not fully understood." (page 2 of 3). "Since the underlying mechanisms that cause IBS are not yet understood, treatment typically targets the symptoms. Unfortunately, even this can be difficult, since people have varying symptoms, either alternating or concurrently... Medications can be an important part of relieving symptoms in more severe cases, but no single medication or combination of medication works for everyone with IBS.

Additionally, Applicant's elected species of protease inhibitor, INVIRASE® is not known in the art to be used for IBD, as it is only known for use in the treatment of HIV (INVIRASE fact sheet. Roche Laboratories, Inc.(2005) 32 pages).

(5) The relative skill of those in the art:

The relative skill of those in the art is high with regards to formulation, however it is low with regards to formulation of compositions having effective doses for the intended uses recited, and the relative skill in the art is low with regards to knowing *a priori* which compounds, e.g. protease inhibitors, will function in treating a condition they are not otherwise known to treat.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided working examples for treating IBD with OT/S via the model for IBD (e.g. Example 7, pages 58). The specification sets forth a prophetic example for biliary cirrhosis with OT/S (Example 6, page 57).

However, the specification does not provide working examples of any other disorder or condition being treating by OT/S, alone or in combination with any protease inhibitor. The specification does not set forth any examples of using OT/S with any protease inhibitor, including treating IBD with OT/S and INVIRASE®, a protease inhibitor not recognized in the art for treating IBD. Furthermore, the specification fails to set forth guidance on how one would make and use the compositions/kits for treating any of the myriad of disease, as the model for IBD is not recognized as a model for any other disease/condition. Additionally, the specification fails to provide guidance on how one would extrapolate the example for IBD to any of the other recited conditions, when the etiology is unknown, or where the art recognizes that the known treatments are difficult or unsuccessful, or how to extrapolate OT/S treatment of IBD to include treatment of any condition/disease with any protease inhibitor.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above and the high unpredictability in treating the myriad of conditions embraced by the claims, the lack of guidance provided in the specification, one skilled in the art could not practice the invention commensurate in the scope of the claims without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 and 17-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over HOLLANDER in view of NIH News Alert, both presented *supra*, and in further view of SWAIN (E. Swain. Pharmaceutical and Medical Packaging News (1999) 4 pages) and PIERCE (PIERCE Technical Resource Sheet TR0043.0 "Protein Stability and Storage" 6/03, 3 pages).

The instant claims are drawn to compositions of OT/S, kits thereof, for a variety of intended uses, optionally with a protease inhibitor.

Hollander teaches treating autism with oxytocin (claim 1) and that, "Agents suitable for use in combination therapy are any chemical compound or treatment method useful to patients with disorders associated with repetitive behaviors..." (paragraph [0046]).

NIH News Alert teaches treating autism with secretin (e.g. page 2, citing Horvath, et al.).

Swain teaches that packaging of pharmaceuticals can add to the 'bottom line' by reducing theft, counterfeiting, increasing shelf life, and improve patient compliance (page 1 of 4).

PIERCE teaches that protease inhibitors are added to protein solutions to lengthen shelf life (e.g. Table 2, page 2) by preventing cleavage of proteins.

As set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980), "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; the idea of combining them flows logically from their having been individually taught in prior art." Thus, because both oxytocin and secretin have been taught in the prior art as useful for treating autism, it would have been obvious to have combined the two for making a composition for the same purpose.

With regards to the kit, the examiner has interpreted 'kit' broadly to include packaging for sale. It would have been obvious at the time of the invention to have packaged the pharmaceutical composition in any packaging for the benefit of reducing theft, reducing counterfeiting and increasing shelf life of the compound, as well as for the benefit of product recognition during sales of the product. One would have been motivated to have packaged the pharmaceutical for the benefit of, but not limited to, increasing shelf life of the compound and to increase the product visibility. One would have had a reasonable expectation for success in packaging the pharmaceutical in order to prolong the shelf life, as packaging pharmaceuticals is widely practiced in the formulary arts in order to generate sales.

Furthermore, it would have been obvious to have added into the composition and/or kit a protease inhibitor to prevent protein degradation/cleavage during storage to increase the shelf life. One would have been motivated to have added a protease inhibitor to the composition/kit because oxytocin and secretin are both peptide compounds, susceptible to proteolysis, and to increase the shelf life of the peptides in the composition. One would have had a reasonable expectation for success in making the composition/kit with a protease inhibitor as PIERCE teaches protease inhibitors are added to prevent proteolytic cleavage of peptides during storage and to increase the shelf life.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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